Letter to the Editor

Risk of Phenotypic Abnormalities in Paracentric Inversion Carriers

To the Editor:

We would like to draw your readers' attention to potentially misleading information contained in a paper by Pettenati et al. [1995].

This paper reviews 446 cases of paracentric inversions from both the literature and the authors' own experience. Page 178 of the paper states that a "strong association between PAI [paracentric inversions] and MR/MCA [mental retardation and/or congenital anomalies] (22.2%) was observed in this review" and that "these observations suggest a 10–20% association between PAI and mental retardation and/or phenotypic abnormalities." Later, this is expanded to: "PAI identified de novo were more likely to be associated with MR/MCA (31.6%) than inherited PAI (22%)."

These statements could be reasonably interpreted to imply at least a 20% risk for MR/MCA in cases of PAI identified at amniocentesis, whether inherited or de novo. However, the data in the paper do not support this interpretation. The figures quoted above refer to the *proportion of cases ascertained because of MR/MCA* as shown in Table IV of the paper. This cannot be used to imply an association between abnormalities and PAI, or to provide an estimate of risk, since there is both a reporting bias in the cases in the literature, and an ascertainment bias in the cases collected by the authors. Because we do not usually perform chromosome analysis on normal children, cases of paracentric inversions identified in cytogenetics laboratories and/or reported in the literature will underrepresent normal individuals. The situation is analogous to the previous confusion about the outcome of sex chromosome anomalies because of the way they were originally ascertained.

The cases ascertained "incidentally" (and most particularly those identified prenatally) are those from which we could obtain a relatively unbiased estimate of any association with abnormalities. Unfortunately, the authors do not provide these data from their series of cases, for either inherited or de novo inversions. It would be good to have this information, to add to the small series previously collected [Warburton, 1991], where 3 of 32 inversions (both paracentric and pericentric) ascertained prenatally were reported to have congenital abnormalities at birth. Until we have more data it is, in our opinion, best to use the overall risk for two-break rearrangements (6.7%) from the above paper for counseling parents when a de novo inversion is detected in amniotic fluid. There is no reason to believe that the risk for inherited inversions is significantly increased over background.

REFERENCES

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Warburton D (1991): De novo balanced chromosome rearrangements and extra marker chromosomes identified at prenatal diagnosis: Clinical significance and distribution of break points. Am J Hum Genet 49:995–1013.

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